

Appendix 5 (as supplied by the authors): Summary of findings for additional outcomes at 6-months

Outcome	Intervention and Comparison intervention	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Quality of evidence (GRADE)	Comments
		Assumed risk (with comparator)	Corresponding risk (with intervention)				
ACR50 at 6 months by DRUG*studies							
Abatacept	Abatacept + DMARD/Biologic vs placebo + DMARD/Biologic	137 per 1000	338 per 1000 (274 to 421)	RR 2.47 (2 to 3.07)	1648 (5 studies W2-6*)	⊕⊕⊕⊖ moderate ¹	
Adalimumab	Adalimumab +/- DMARD/Biologic vs placebo +/- DMARD/Biologic	109 per 1000	380 per 1000 (258 to 559)	RR 3.49 (2.37 to 5.13)	1195 (4 studies W10-12,15*)	⊕⊕⊕⊖ moderate ^{2a}	
	Adalimumab vs placebo	73 per 1000	232 per 1000 (142 to 382)	RR 3.18 (1.94 to 5.23)	506 (3 studies W10,13,15*)	⊕⊕⊕⊖ moderate ^{2b}	
Anakinra	Anakinra + DMARD vs placebo + DMARD	74 per 1000	186 per 1000 (115 to 298)	RR 2.51 (1.56 to 4.03)	654 (2 studies W18,19*)	⊕⊕⊕⊖ moderate ³	
	Anakinra + Biologic vs placebo + Biologic	412 per 1000	310 per 1000	RR 0.75 (0.49 to 1.14)	161 (1 study W20*)	⊕⊕⊕⊖ moderate ⁴	
Etanercept	Etanercept +/- DMARD vs placebo +/- DMARD	45 per 1000	400 per 1000 (162 to 985)	RR 8.89 (3.61 to 21.89)	247 (2 studies W21,22*)	⊕⊕⊕⊖ moderate ⁵	
Rituximab	Rituximab + DMARD	85 per 1000	316 per 1000 (218 to 457)	RR 3.72 (2.57 to 5.38)	823 (3 studies)	⊕⊕⊕⊖ moderate ⁶	

	vs placebo + DMARD				W29-31*)	
DAS low disease activity at 6 months by DRUG*studies						
Abatacept	Abatacept + DMARD/Biologic vs placebo + DMARD/Biologic	75 per 1000	252 per 1000 (171 to 372)	RR 3.36 (2.28 to 4.96)	1027 (2 studies W2,5*)	⊕⊕⊕⊖ moderate ¹
Physical function - HAQ at 6 months by DRUG*studies						
Adalimumab	Adalimumab +/- DMARD/Biologic vs placebo +/- DMARD/Biologic	The mean change in the control groups was -0.24 points	The mean change in the intervention groups was -0.56 points	PDC*** 182% improvement	663 (3 studies W11,12,15*)	⊕⊕⊕⊖ moderate ^{7a}
	Adalimumab vs placebo	The mean change in the control groups was -0.07	The mean change in the intervention groups was -0.38 points	PDC*** 25% improvement	401 (2 studies W13,14*)	⊕⊕⊕⊖ moderate ^{7b}
Anakinra	Anakinra + DMARD vs placebo + DMARD	The mean change in the control groups was -0.18 points	The mean change in the intervention groups was -0.37 points	PDC*** 61% improvement	951 (2 studies W16,19*)	⊕⊕⊕⊖ low ^{8,9}
Etanercept	Etanercept +/- DMARD vs placebo +/- DMARD	The mean change in the control group was -0.4 points	The mean change in the intervention group was -0.7 points	PDC*** 75% improvement	89 (1 study W22*)	⊕⊕⊕⊕ high

Rituximab	Rituximab + DMARD vs placebo + DMARD	The mean change in the control groups was -0.16 points	The mean change in the intervention group was -0.47 points	PDC*** 182% improvement	823 (3 studies W29-31*)	⊕⊕⊕⊖ moderate ⁶
Radiographic score (total) at 6 months by DRUG*studies						
Anakinra (Larsen score)	Anakinra + DMARD vs placebo + DMARD	The mean change in the control group was 6.4 points	The mean change in the intervention group was 3.9 points	PDC** 39.1% less progression	172 (1 study W16*)	⊕⊕⊕⊖ moderate ¹⁰
AE (total) at 6 months by DRUG*studies						
Abatacept	Abatacept + DMARD/Biologic vs placebo + DMARD/Biologic	770 per 1000	816 per 1000 (747 to 885)	RR 1.06 (0.97 to 1.15)	657 (2 studies W2,3*)	⊕⊕⊕⊖ moderate ¹¹
Adalimumab	Adalimumab +/- DMARD/Biologic vs placebo +/- DMARD/Biologic	893 per 1000	920 per 1000 (893 to 947)	RR 1.03 (1 to 1.06) ¹²	1987 (6 studies W8-12,32*)	⊕⊕⊕⊖ low ^{12a,13}
	Adalimumab vs placebo	779 per 1000	974 per 1000 (748 to 1000)	RR 1.25 (0.96 to 1.61)	854 (3 studies W10,13,14*)	⊕⊕⊕⊖ low ^{12b,13}
Anakinra	Anakinra + DMARD vs placebo + DMARD	879 per 1000	923 per 1000 (826 to 1000)	RR 1.05 (0.94 to 1.17)	1894 (2 studies W17,19*)	⊕⊕⊕⊖ moderate ³
	Anakinra + Biologic vs placebo + Biologic	973 per 1000	1000 per 1000 (924 to 1000)	RR 1.04 (0.95 to 1.14)	155 (1 study W20*)	⊕⊕⊕⊖ moderate ⁴

Rituximab	Rituximab + DMARD vs placebo + DMARD	804 per 1000	860 per 1000 (732 to 1000)	RR 1.07 (0.91 to 1.26)	938 (3 studies W29-31*)	⊕⊕⊕⊖ low ^{6,11}
SAE (total) at 6 months for rheumatoid arthritis						
Abatacept	Abatacept + DMARD/Biologic vs placebo + DMARD/Biologic	97 per 1000	78 per 1000 (48 to 127)	RR 0.8 (0.49 to 1.31)	703 (2 studies W2,3*)	⊕⊕⊕⊕ high
Adalimumab	Adalimumab +/- DMARD/Biologic vs placebo +/- DMARD/Biologic	90 per 1000	84 per 1000 (67 to 131)	RR 0.93 (0.60 to 1.45)	843 (4 studies W8,10,12,32*)	⊕⊕⊕⊖ low ^{13,14}
	Adalimumab vs placebo	105 per 1000	111 per 1000 (69 to 179)	RR 1.06 (0.66 to 1.7)	1111 (4 Studies W10,13,14,33*)	⊕⊕⊕⊖ low ^{12b,13}
Anakinra	Anakinra + DMARD vs placebo + DMARD	56 per 1000	86 per 1000 (38 to 195)	RR 1.53 (0.67 to 3.48)	1900 (2 studies W17,19*)	⊕⊕⊕⊖ moderate ³
	Anakinra + Biologic vs placebo + Biologic	25 per 1000	148 per 1000 (34 to 641)	RR 5.93 (1.37 to 25.64)	161 (1 study W20*)	⊕⊕⊕⊖ low ^{4,5}
Rituximab	Rituximab + DMARD vs placebo + DMARD	70 per 1000	71 per 1000 (45 to 113)	RR 1.01 (0.64 to 1.61)	938 (3 studies W2-4*)	⊕⊕⊕⊖ moderate ⁶
Total withdrawals at 6 months- by DRUG*studies						
Abatacept	Abatacept + DMARD/Biologic	235 per 1000	148 per 1000 (94 to 237)	RR 0.63 (0.4 to 1.01)	891 (3 studies)	⊕⊕⊕⊕ high

	vs placebo + DMARD/Biologic				W2-4*)	
Adalimumab	Adalimumab +/- DMARD/Biologic vs placebo +/- DMARD/Biologic	261 per 1000	204 per 1000 (172 to 240)	RR 0.78 (0.66 to 0.92)	1964 (7 studies W8-12,15,32*)	⊕⊕⊕⊕ low ^{13,15}
	Adalimumab vs placebo	345 per 1000	190 per 1000 (117 to 310)	RR 0.55 (0.34 to 0.9)	1180 (3 studies W13,14,33*)	⊕⊕⊕⊕ low ^{13,16}
Anakinra	Anakinra + DMARD vs placebo + DMARD	222 per 1000	231 per 1000 (191 to 282)	RR 1.04 (0.86 to 1.27)	1957 (3 studies W16-18*)	⊕⊕⊕⊕ moderate ^{3,10}
	Anakinra + Biologic vs placebo + Biologic	62 per 1000	184 per 1000 (70 to 482)	RR 2.96 (1.13 to 7.77)	162 (1 study W20*)	⊕⊕⊕⊕ moderate ⁴
Etanercept	Etanercept +/- DMARD vs placebo +/- DMARD	545 per 1000	185 per 1000 (120 to 272)	RR 0.34 (0.22 to 0.5)	247 (2 studies W21,22*)	⊕⊕⊕⊕ high
Rituximab	Rituximab + DMARD vs placebo + DMARD	379 per 1000	148 per 1000 (117 to 186)	RR 0.39 (0.31 to 0.49)	938 (3 studies W29-31*)	⊕⊕⊕⊕ moderate ⁶

Assumed Risk (Score) is the change score of the most representative study in the control group.

The Corresponding Risk (Score) is the change score in the intervention group.

DMARD = disease-modifying anti-rheumatic drugs; AE = adverse events; SAE = serious adverse events; DAS = disease activity score; HAQ = Health Assessment Questionnaire; RR = risk ratio

*** PDC = percent difference in improvement in physical function between the treatment and control groups relative to improvement in control group.

**PDC = percent difference in radiographic progression between the treatment and control group relative to progression in control group.

*= references to the studies in the reviews included for analyses in the original reviews (see reference list for details).

¹ Kremer 2006: intention to treat analysis not performed - 9 patients in abatacept group and 5 in control group not included in analysis.

^{2a} Randomization and blinding were not described and also allocation concealment was not clear in four studies: Furst 2003, Keystone 2004; Kim 2007; Weinblatt 2003.

^{2b} Randomization and blinding were not described and also allocation concealment was not clear in three studies: Weinblatt 2003; Miyasaka 2008; van de Putte 2004.

³ Randomization not described in both studies (Cohen 2002; Cohen 2004) ; intention to treat analysis not performed in Cohen 2004 study; blinding not described and >20% dropout in Cohen 2002 study.

⁴ Genovese 2004: allocation concealment not described and ITT analysis not performed.

⁵ Wide confidence interval.

⁶ Randomization and allocation concealment not described in all three studies; blinding not clear in Emery (DANCER) 2006; Attrition not clear in Cohen (REFLEX) 2006 study.

^{7a} Randomization and blinding were not described and also allocation concealment was not clear in all three studies: Keystone 2004; Kim 2007; Weinblatt 2003.

^{7b} Randomization and blinding were not described and also allocation concealment was not clear in both studies: Miyasaka 2008, van de Putte 2004.

⁸ Randomization not described and intention to treat analysis not performed in both studies (Bresnihan 1998; Cohen 2004);

⁹ Bresnihan 1998: non-standard dose included.

¹⁰ Bresnihan 1998: randomization not described and intention to treat analysis not performed.

¹¹ Unexplained heterogeneity.

^{12a} Randomization and blinding were not described and also allocation concealment was not clear in five studies: Breedveld 2007; Furst 2003; Keystone 2004; Kim 2007; Rau 2004.

^{12b} Randomization and blinding were not described and also allocation concealment was not clear in three studies: Furst 2003; Miyasaka 2008; van de Putte 2004.

¹³ Analysis includes non-standard doses.

¹⁴ Randomization and blinding were not described and also allocation concealment was not clear in three studies: Furst 2003; Kim 2007; Rau 2004.

¹⁵ Randomization and blinding were not described and also allocation concealment was not clear in four studies: Breedveld 2007; Furst 2003; Keystone 2004; Kim 2007.